AMENDMENTS MADE TO THE SPECIFICATION

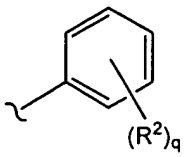
On pages 7-16 of the Specification, please replace paragraphs [0025]-[0080] with the following amended paragraphs.

[0025] Embodiment [0025]: In one example, the compound is according to Formula I~~paragraph [0024]~~, wherein [[M^3]]M^4 is -CH_2-.

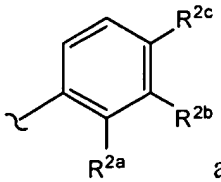
[0026] Embodiment [0026]: In another example, the compound is according to ~~paragraph~~Embodiment [0025], wherein Z is -NR^5-.

[0027] Embodiment [0027]: In another example, the compound is according to ~~paragraph~~Embodiment [0026], wherein R^1 is CH_3-.

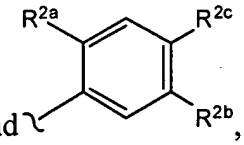
[0028] Embodiment [0028]: In another example, the compound is according to ~~paragraph~~Embodiment [0027], wherein



of **I** is selected from:



and



, wherein R^{2a} is selected from -H, F, Cl, and Br; and R^{2b} and R^{2c} are each independently selected from F, Cl, and Br.

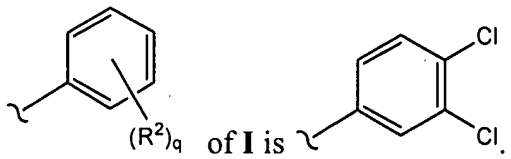
[0029] Embodiment [0029]: In one example, the compound is according to ~~paragraph~~Embodiment [0028], wherein M^2 is a monocyclic five- to seven-membered heterocyclyl or a five- to six-membered heteroaryl, each optionally substituted with between one and three of R^{50}.

[0030] Embodiment [0030]: In another example, the compound is according to ~~paragraph~~Embodiment [0029], wherein M^2 is selected from the group consisting of morpholinyl, thiazolyl, oxadiazolyl, tetrahydropyranyl, and oxazepanyl, each optionally substituted with between one and three of R^{50}.

[0031] Embodiment [0031]: In another example, the compound is according to ~~paragraph~~Embodiment [0030], wherein M^1 is selected from the group consisting of -H,

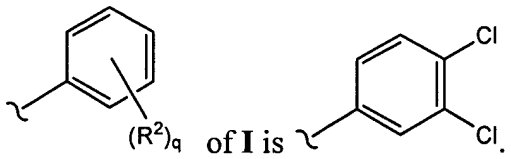
dimethylaminomethyl, ~~(4-methylpiperizin-1-yl)methyl,~~ (4-methylpiperazin-1-yl)methyl, piperidinyl, 1-methylpiperidin-4-yl, morpholin-4-ylmethyl, and phenylmethyl.

[0032] Embodiment [0032]: In another example, the compound is according to ~~paragraph~~Embodiment [0031], wherein

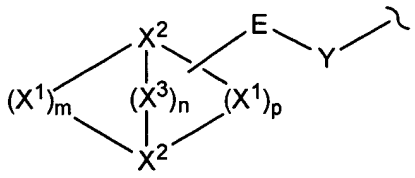


[0033] Embodiment [0033]: In another example, the compound is according to ~~paragraph~~Embodiment [0028], wherein M^1 is either a three- to seven-membered saturated carbocyclyl or a heterocyclyl with one or two annular heteroatoms, wherein the either of the aforementioned are optionally substituted with at least one of C_1-C_3 alkyl, C_1-C_3 alkoxy, C_1-C_3 hydroxyalkyl, $R^{10}(R^{11})N$-, and hydroxy, provided there are no geminal heteroatom substitutions; and wherein $R^{10}$and R^{11} are each independently C_1-C_3 alkyl.

[0034] Embodiment [0034]: In another example, the compound is according to ~~paragraph~~Embodiment [0033], wherein



[0035] Embodiment [0035]: In another example, the compound is according to ~~paragraph~~Embodiment [0024], wherein M^1-M^2-M^3-M^4- together are according to formula **II**;



II

wherein X^1, X^2, and optionally X^3, represent the atoms of a saturated bridged ring system, said saturated bridged ring system containing up to three annular heteroatoms represented by any of X^1, X^2, and X^3; wherein,

each X^1 is independently selected from $-C(R^6)R^7-$, -O-, $-S(O)_{0-2}-$, and $-NR^8-$;

each X^2 is independently a bridgehead methine optionally substituted with R^6, or a bridgehead nitrogen;

each X^3 is independently selected from $-C(R^6)R^7-$, -O-, $-S(O)_{0-2}-$, and $-NR^8-$;

provided, for X^1, X^2, and X^3, there are no nitrogen-nitrogen annular bonds nor geminal di-nitrogen substitutions;

E is selected from $-NR^9-$, -O-, and absent;

Y is either:

a C_{1-3} alkylene linker, between the oxygen at the 7-position of the quinazoline ring system of **I** and either E, or when E is absent, any ring atom of the saturated bridged ring system except X^2, when X^2 is a bridgehead nitrogen; provided there are at least two carbon atoms between the oxygen at the 7-position of the quinazoline ring system of **I** and either E, or when E is absent, any heteroatom represented by X^1, X^2 or X^3; or

Y is absent, when Y is absent, E is also absent; said saturated bridged ring system is directly attached to the oxygen at the 7-position of the quinazoline ring system of **I** via a carbon atom of said saturated bridged ring system;

m and p are each independently between one and four;

n is between zero and two, when n is zero, then there is a direct single bond between the two bridgehead X^2's;

R^6 and R^7 are each independently selected from -H, halogen, trihalomethyl, -CN, $-NH_2$, $-NO_2$, $-OR^3$, $-N(R^3)R^4$, $-S(O)_{0-2}R^4$, $-SO_2N(R^3)R^4$, $-CO_2R^3$, $-C(O)N(R^3)R^4$,

$-N(R^3)SO_2R^4$, $-N(R^3)C(O)R^3$; $-NCO_2R^3$, $-C(O)R^3$, optionally substituted lower alkyl, optionally substituted aryl, optionally substituted lower arylalkyl, optionally substituted heterocyclyl, optionally substituted lower heterocyclylalkyl; or

R^6 and R^7, when taken together are oxo; or

R^6 and R^7, when taken together with a common carbon to which they are attached, form a optionally substituted three- to seven-membered spirocyclyl, said optionally substituted three- to seven-membered spirocyclyl optionally containing at least one additional heteroatom selected from N, O, S, and P; and

R^8 is selected from R^3, $-SO_2N(R^3)R^4$, $-CO_2R^3$, $-C(O)N(R^3)R^4$, $-SO_2R^4$, and $-C(O)R^3$.

with the proviso that when Y is a C_{1-3} alkylene linker; E is absent, Z is -NH- or $-N(CH_3)$-; R^1 is a C_{1-3} alkyl; R^2 is -H or halogen; n = 0; and, the atoms, X^1, of one bridge of the saturated bridged ring system, when combined with both bridgehead atoms, X^2, of the saturated bridged ring system, represent:

either a pyrrolidine ring or a piperidine ring, and any atom, X^1 or X^2, of either of said pyrrolidine ring or said piperidine ring is attached to Y, then the other bridge of said saturated bridged ring system cannot be any one of $-OC(O)CH_2$-, $-CH_2OC(O)$-, $-OC(O)CH_2CH_2$-, $-CH_2OC(O)CH_2$-, $-CH_2CH_2OC(O)$-, $-OC(O)CH_2NH$-, $-OC(O)CH_2N(C_{1-4}alkyl)$-, and $-OC(O)CH_2O$-; or

either a piperazine ring or a 4-(C_{1-4} alkyl)-piperazine ring, and any atom, X^1 or X^2, of either of said piperazine ring or said 4-(C_{1-4} alkyl)-piperazine ring is attached to Y, then the other bridge of said saturated bridged ring system, only when attached via the 2- and the 3-position of either of said piperazine ring or said 4-(C_{1-4} alkyl)-piperazine ring, cannot be one of $-CH_2OC(O)CH_2$-, $-CH_2CH_2OC(O)$-, and either of the two aforementioned bridges optionally substituted by one or two C_{1-2}alkyl groups; or

a piperazine ring, and any atom, X^1 or X^2, of said piperazine ring is attached to Y, then the other bridge of said saturated bridged ring system, only

when attached via the 3- and the 4-position of said piperazine ring, cannot be one of -C(O)OCH$_2$CH$_2$-, -CH$_2$OC(O)CH$_2$-, and either of the two aforementioned bridges optionally substituted by one or two C$_{1-2}$ alkyl groups, and only when either of the two aforementioned bridges are attached to the 3-position of said piperazine ring via their left-hand end as depicted above; or

a 2-oxomorpholine ring, said 2-oxomorpholine ring attached to Y via its 4-position, then the other bridge of said saturated bridged ring system, only when attached via the 5- and the 6-position of said 2-oxomorpholine ring, cannot be one of -(CH$_2$)$_g$-, -CH$_2$WCH$_2$-, -CH$_2$WCH$_2$CH$_2$-, and -CH$_2$CH$_2$WCH$_2$-, wherein W is -O-, -S(O)$_{0-2}$-, -NH-, or -N(C$_{1-4}$ alkyl)- wherein g is 2, 3, or 4.

[0036] Embodiment [0036]: In one example, the compound is according to ~~paragraph~~Embodiment [0035], wherein Z is -NR^5-.

[0037] Embodiment [0037]: In another example, the compound is according to ~~paragraph~~Embodiment [0036], wherein R^2 is selected from -H, halogen, trihalomethyl, -CN, -NO$_2$, -OR^3, and optionally substituted lower alkyl.

[0038] Embodiment [0038]: In another example, the compound is according to ~~paragraph~~Embodiment [0037], wherein R^1 is an unsubstituted C$_{1-3}$ alkyl.

[0039] Embodiment [0039]: In another example, the compound is according to ~~paragraph~~Embodiment [0038], wherein the saturated bridged ring system has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], [3.1.0], [3.3.3], [3.3.2], [3.3.1], [3.2.2], [3.2.1], [2.2.2], and [2.2.1].

[0040] Embodiment [0040]: In another example, the compound is according to ~~paragraph~~Embodiment [0039], wherein Y is selected from -CH$_2$CH$_2$-, -CH$_2$-, and absent.

[0041] Embodiment [0041]: In another example, the compound is according to ~~paragraph~~Embodiment [0040], wherein q [[=]]is one, two, or ~~to~~ three.

[0042] Embodiment [0042]: In another example, the compound is according to ~~paragraph~~Embodiment [0041], wherein R^5 is -H.

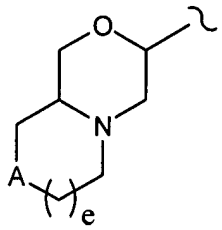
[0043] Embodiment [0043]: In another example, the compound is according to ~~paragraph~~Embodiment [0042], wherein R^1 is methyl.

[0044] Embodiment [0044]: In another example, the compound is according to ~~paragraph~~Embodiment [0043], wherein the saturated bridged ring system has a geometry selected from the group consisting of [4.4.0], [4.3.0], [4.2.0], [4.1.0], [3.3.0], [3.2.0], and [3.1.0].

[0045] Embodiment [0045]: In another example, the compound is according to ~~paragraph~~Embodiment [0044], wherein said saturated bridged ring system contains one or two annular nitrogens, said one or two annular nitrogens are selected from $-NR^8-$, when X^1, and a bridgehead nitrogen, when X^2.

[0046] Embodiment [0046]: In another example, the compound is according to ~~paragraph~~Embodiment [0045], wherein E is absent.

[0047] Embodiment [0047]: In another example, the compound is according to ~~paragraph~~Embodiment [0046], wherein said saturated bridged ring system is according to formula **III**;



III

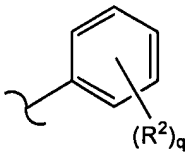
wherein A is selected from -O-, $-S(O)_{0-2}-$, $-NR^8-$, and absent; and e is 0 or 1.

[0048] Embodiment [0048]: In another example, the compounds ~~of are~~ is according to ~~paragraph~~Embodiment [0047], wherein Y is $-CH_2-$.

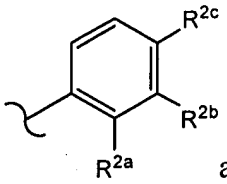
[0049] Embodiment [0049]: In another example, the compound is according to ~~paragraph~~Embodiment [0048], wherein A is selected from $-NR^8-$, wherein R^8 is selected

from -H, optionally substituted lower alkyl, $-CO_2R^3$, $-C(O)N(R^3)R^4$, $-SO_2R^4$, and $-C(O)R^3$; -O-; and absent.

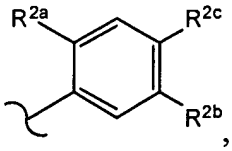
[0050] Embodiment [0050]: In another example, the compound is according to ~~paragraph~~Embodiment [0049], wherein



of **I** is selected from:



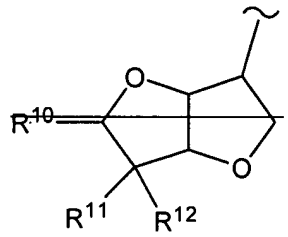
and



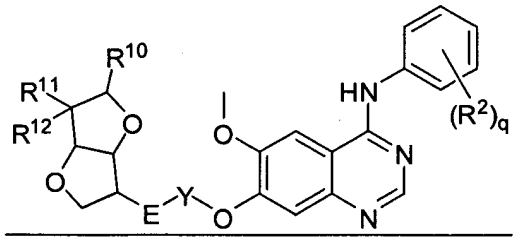
, wherein R^{2a}, R^{2b}, and R^{2c} are each independently selected from F, Cl, and Br.

[0051] Embodiment [0051]: In another example, the compound is according to ~~paragraph~~Embodiment [0050], wherein R^{2a} is F, R^{2b} is Cl, and R^{2c} is either Cl or Br.

[0052] Embodiment [0052]: In another example, the compound is according to Formula Ia~~paragraph [0044], wherein said saturated bridged ring system is according to formula IV~~;:



~~IV~~



Ia

or a pharmaceutically acceptable salt or hydrate thereof, wherein

q is 1, 2, or 3;

R^2 is selected from -H, halogen, trihalomethyl, -CN, $-NO_2$, $-OR^3$, and optionally substituted lower alkyl;

E is selected from $-NR^9-$, -O-, and absent;

Y is selected from $-CH_2CH_2-$, $-CH_2-$, and absent;

R^{10} is selected from -H, optionally substituted alkyl, and $-OR^{13}$; and R^{11} and R^{12} are each independently selected from -H, $-CF_3$, -F, $-N(R^3)R^4$, $-N(C=O)R^3$, $-N(R^3)SO_2R^3$, $-S(O)_{0-2}R^{13}$, and $-OR^{13}$; or

R^{10} is selected from -H, and $-OR^{13}$; and R^{11} and R^{12}, when taken together, are oxo, exo-alkenyl, or when taken together with the carbon to which they are attached, form a three- to seven-membered spirocyclyl;

R^{13} is selected from -H, $-C(=O)R^4$, optionally substituted lower ~~alkylidyne~~alkynyl, optionally substituted lower ~~arylalkylidyne~~arylalkynyl, optionally substituted lower ~~heterocyclylalkylidyne~~heterocyclylalkynyl, optionally substituted lower ~~alkylidene~~alkenyl, optionally substituted lower ~~arylalkylidene~~arylalkynyl, optionally substituted lower ~~heterocyclylalkylidene~~heterocyclylalkynyl, optionally substituted lower alkyl, optionally substituted lower arylalkyl, optionally substituted aryl, optionally substituted lower heterocyclylalkyl, and optionally substituted heterocyclyl; or

~~or~~ two R^{13}'s, when taken together, form 1) a corresponding spirocyclic ketal from R^{11}, R^{12} and the carbon to which they are attached, when R^{11} and R^{12} are both $-OR^{13}$, or 2) a corresponding cyclic ketal from R^{10} and one of R^{11} and R^{12}, and the corresponding carbons to which they are attached, when R^{10} is $-OR^{13}$, and at least one of R^{11} and R^{12} is also $-OR^{13}$.

[0053] Embodiment [0053]: In another example, the compounds ~~of are~~ is according to ~~paragraph~~Embodiment [0052], wherein Y is either $-CH_2-$ or absent.

[0054] Embodiment [0054]: In another example, the compounds ~~of are~~ is according to ~~paragraph~~Embodiment [0053], wherein one of R^{11} and R^{12} is $-OR^{13}$, wherein R^{13} is selected from -H, $-C(O)R^4$, and optionally substituted lower alkyl; and R^{10} and the other of R^{11} and R^{12} are both -H.

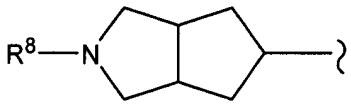
[0055] Embodiment [0055]: In another example, the compounds ~~of are~~ is according to ~~paragraph~~Embodiment [0053], wherein one of R^{11} and R^{12} is -F; and R^{10} and the other of R^{11} and R^{12} are both -H.

[0056] Embodiment [0056]: In another example, the compounds ~~of are~~ is according to ~~paragraph~~Embodiment [0053], wherein R^{13} is an alkyl group containing at least one fluorine substitution thereon.

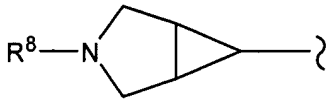
[0057] Embodiment [0057]: In another example, the compound is according to ~~paragraph~~Embodiment [0053], wherein q is two or three.

[0058] Embodiment [0058]: In another example, the compound is according to ~~paragraph~~Embodiment [0057], wherein each R^2 is independently selected from -F, -Cl, -Br, $-CF_3$, $-CH_3$, and $-OR^{25}$; wherein R^{25} is either methyl or aryl, each optionally substituted with one to three halogens.

[0059] Embodiment [0059]: In another example, the compound is according to ~~paragraph~~Embodiment [0045], wherein said saturated bridged ring system is according to either formula **V** or formula **VI**;



V

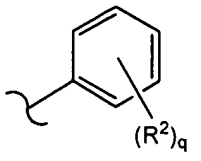


VI

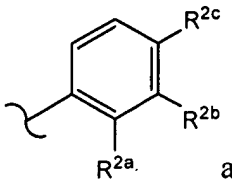
wherein R^8 is selected from -H, optionally substituted lower alkyl, $-CO_2R^3$, $-C(O)N(R^3)R^4$, $-SO_2R^4$, and $-C(O)R^3$.

[0060] Embodiment [0060]: In another example, the compound is according to ~~paragraph~~Embodiment [0059], wherein Y is either $-CH_2-$ or absent.

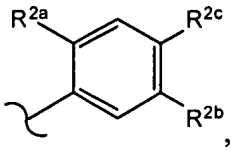
[0061] Embodiment [0061]: In another example, the compound is according to ~~paragraph~~Embodiment [0060], wherein



of **I** is selected from:



and

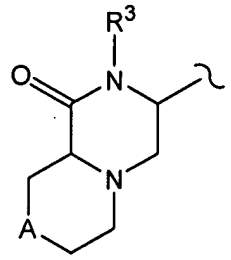


, wherein R^{2a}, R^{2b}, and R^{2c} are each independently selected from F, Cl, and Br.

[0062] Embodiment [0062]: In another example, the compound is according to ~~paragraph~~Embodiment [0061], wherein R^{2a} is F, R^{2b} is Cl, and R^{2c} is either Cl or Br.

[0063] Embodiment [0063]: In another example, the compound is according to ~~paragraph~~Embodiment [0062], wherein R^{8} is methyl or ethyl.

[0064] Embodiment [0064]: In another example, the compound is according to ~~paragraph~~Embodiment [0046], wherein said saturated bridged ring system is according to formula **VII**;



VII

wherein A is selected from -O-, -$S(O)_{0-2}$-, -NR^{8}-, -$CR^{6}R^{7}$-, and absent.

[0065] Embodiment [0065]: In another example, the compound is according to ~~paragraph~~Embodiment [0064], wherein R^{3} is selected from -H and optionally substituted alkyl.

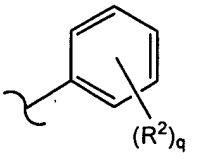
[0066] Embodiment [0066]: In another example, the compound is according to ~~paragraph~~Embodiment [0065], wherein A is either -$C(R^{6})R^{7}$- or absent.

[0067] Embodiment [0067]: In another example, the compound is according to ~~paragraph~~Embodiment [0066], wherein A is either -CH_2- or absent.

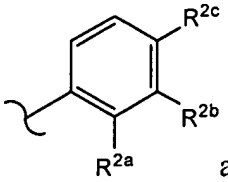
[0068] Embodiment [0068]: In another example, the compounds ~~of are~~ is according to ~~paragraph~~Embodiment [0067], wherein Y is $-CH_2-$.

[0069] Embodiment [0069]: In another example, the compound is according to ~~paragraph~~Embodiment [0068], wherein q [[=]]is 3.

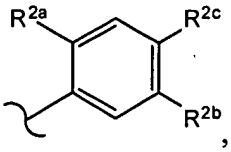
[0070] Embodiment [0070]: In another example, the compound is according to ~~paragraph~~Embodiment [0069], wherein



of **I** is selected from:



and



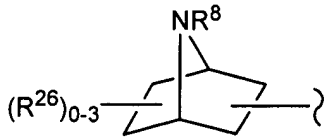
, wherein R^{2a}, R^{2b}, and R^{2c} are each independently selected from F, Cl, and Br.

[0071] Embodiment [0071]: In another example, the compound is according to ~~paragraph~~Embodiment [0070], wherein R^{2a} is F, R^{2b} is Cl, and R^{2c} is either Cl or Br.

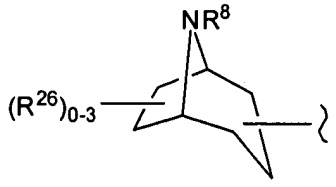
[0072] Embodiment [0072]: In another example, the compound is according to ~~paragraph~~Embodiment [0043], wherein the saturated bridged ring system has a geometry selected from the group consisting of [3.3.1], [3.2.1], and [2.2.1].

[0073] Embodiment [0073]: In another example, the compound is according to ~~paragraph~~Embodiment [0072], wherein said saturated bridged ring system contains one or two annular nitrogens, said one or two annular nitrogens are selected from $-NR^8-$, when X^1, and a bridgehead nitrogen, when X^2.

[0074] Embodiment [0074]: In another example, the compound is according to ~~paragraph~~Embodiment [0073], wherein said saturated bridged ring system is according to formula **VIII** or formula **IX**;



VIII



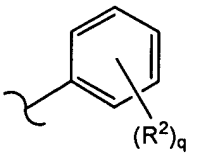
IX

wherein R^8 is selected from -H, optionally substituted lower alkyl, $-CO_2R^3$, $-C(O)N(R^3)R^4$, $-SO_2R^4$, and $-C(O)R^3$; and R^{26} is C_{1-3} alkyl.

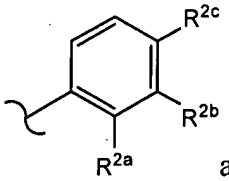
[0075] Embodiment [0075]: In another example, the compound is according to ~~paragraph~~Embodiment [0074], wherein Y is $-CH_2CH_2-$; and E is either absent or $-N(R^9)-$.

[0076] Embodiment [0076]: In another example, the compound is according to ~~paragraph~~Embodiment [0075], wherein q is[[=]] 3.

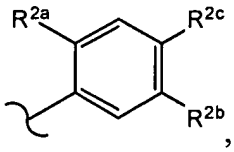
[0077] Embodiment [0077]: In another example, the compound is according to ~~paragraph~~Embodiment [0076], wherein



of **I** is selected from:



and



, wherein R^{2a}, R^{2b}, and R^{2c} are each independently selected from F, Cl, and Br.

[0078] Embodiment [0078]: In another example, the compound is according to ~~paragraph~~Embodiment [0077], wherein R^{2a} is F, R^{2b} is Cl, and R^{2c} is either Cl or Br.

[0079] Embodiment [0079]: In another example, the compound is according to ~~paragraph~~Embodiment [0078], wherein R^8 is methyl or ethyl.

[0080] Embodiment [0080]: In another example, the compound is according to Formula I or Ia~~paragraph [0024]~~, selected from Table 1:

Please replace entries 1-4, 6-17, 22-24, 26-28, and 31 in Table 1 found on pages 16-20 of the Specification with the following.

Table 1

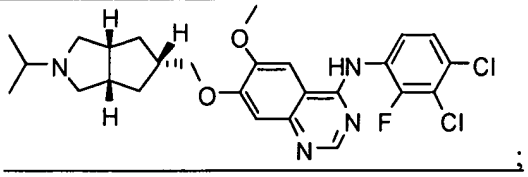
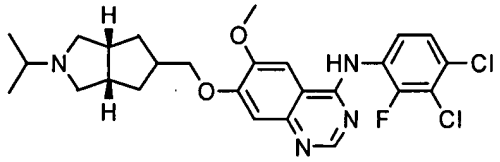
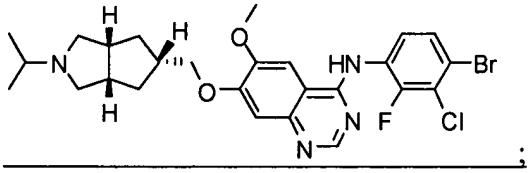
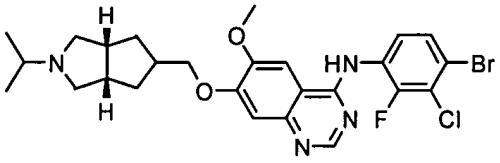
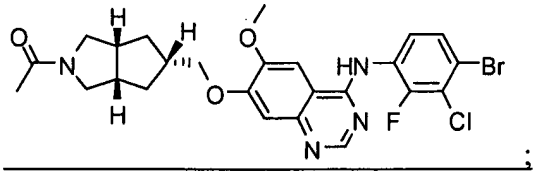
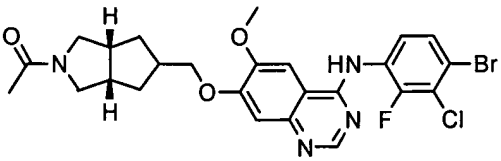
Entry	Name	Structure
1	N-(3,4-dichloro-2-fluorophenyl)-7-({[(3aR,5r,6aS)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(3,4-dichloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	 ; 
2	N-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3aR,5r,6aS)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-(1-methylethyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	 ; 
3	7-({[(3aR,5r,6aS)-2-acetyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)quinazolin-4-amine; 7-({[(3aR,6aS)-2-acetyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)quinazolin-4-amine	 ; 

Table 1

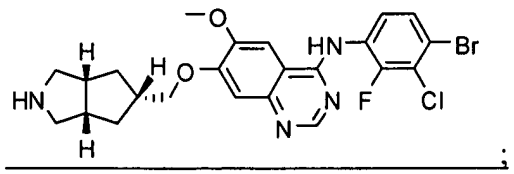
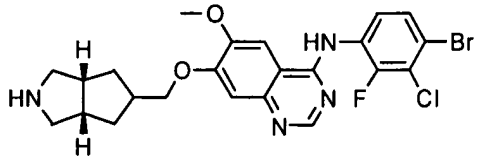
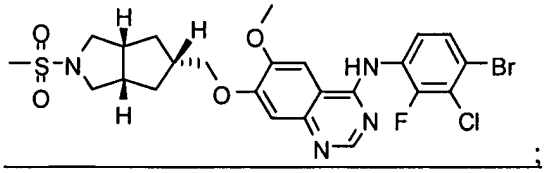
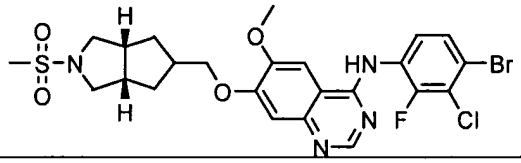
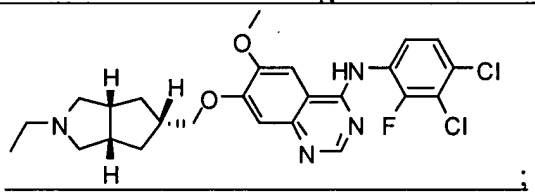
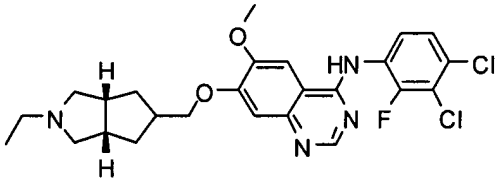
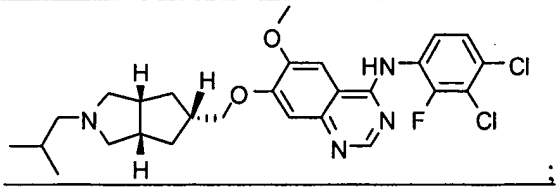
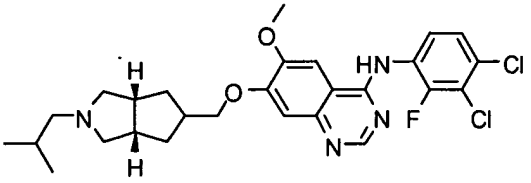
4	N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3aR,5r,6aS)-octahydrocyclopenta[c]pyrrol-5-ylmethyl]oxy}quinazolin-4-amine; N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3aR,6aS)-octahydrocyclopenta[c]pyrrol-5-ylmethyl]oxy}quinazolin-4-amine	 
6	N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3aR,5r,6aS)-2-(methylsulfonyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine; N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3aR,6aS)-2-(methylsulfonyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine	 
7	N-(3,4-dichloro-2-fluorophenyl)-7-({[(3aR,5r,6aS)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(3,4-dichloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	 
8	N-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3aR,5r,6aS)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine; N-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3aR,6aS)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine	 

Table 1

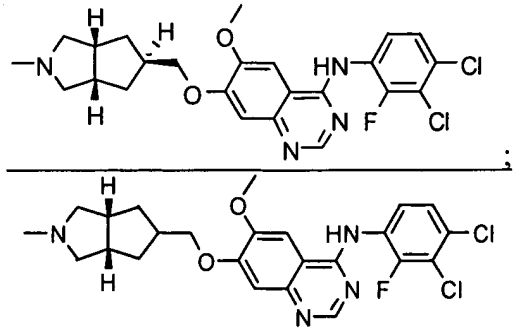
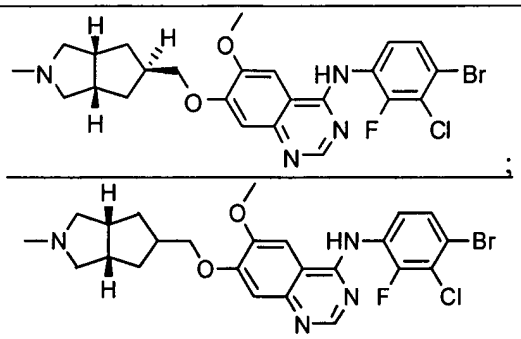
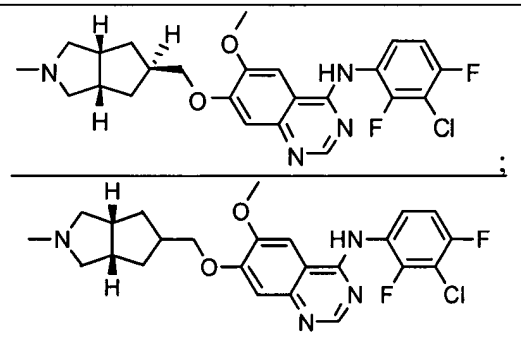
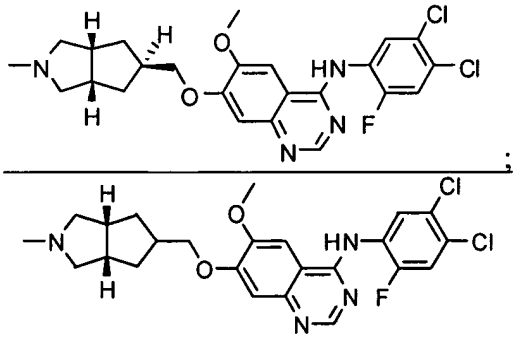
9	N-(3,4-dichloro-2-fluorophenyl)-7-({[(3aR,5s,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(3,4-dichloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	
10	N-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3aR,5s,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	
11	N-(3-chloro-2,4-difluorophenyl)-7-({[(3aR,5s,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(3-chloro-2,4-difluorophenyl)-7-({[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	
12	N-(4,5-dichloro-2-fluorophenyl)-7-({[(3aR,5s,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(4,5-dichloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	

Table 1

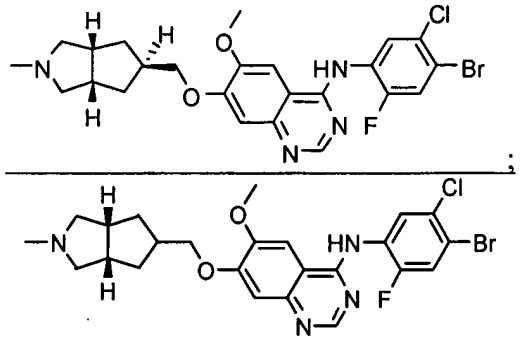
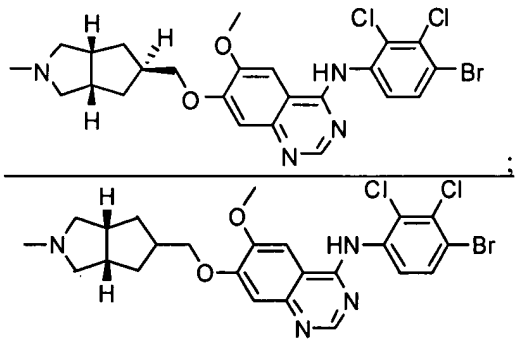
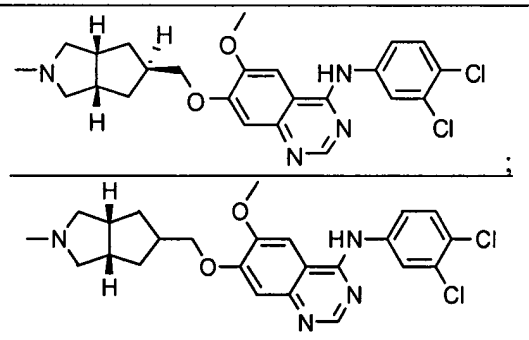
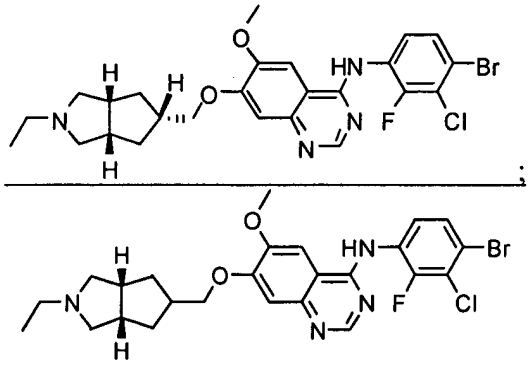
13	N-(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3aR,5s,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(4-bromo-5-chloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	
14	N-(4-bromo-2,3-dichlorophenyl)-7-({[(3aR,5s,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(4-bromo-2,3-dichlorophenyl)-7-({[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	
15	N-(3,4-dichlorophenyl)-7-({[(3aR,5s,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(3,4-dichlorophenyl)-7-({[(3aR,6aS)-2-methyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	
16	N-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3aR,5r,6aS)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine; N-(4-bromo-3-chloro-2-fluorophenyl)-7-({[(3aR,6aS)-2-ethyloctahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)-6-(methyloxy)quinazolin-4-amine	

Table 1

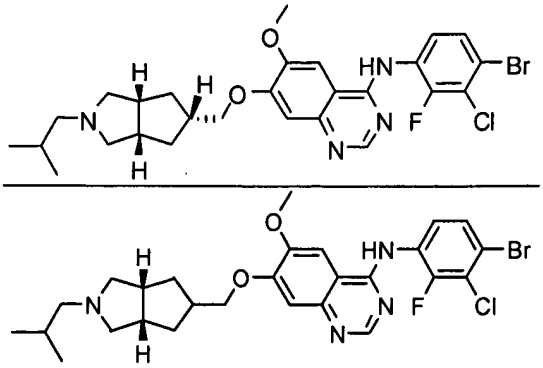
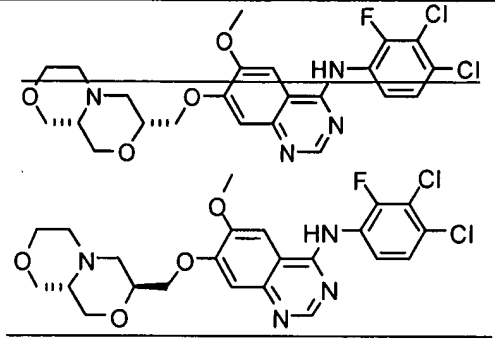
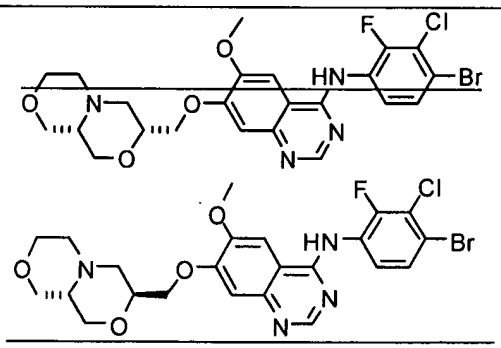
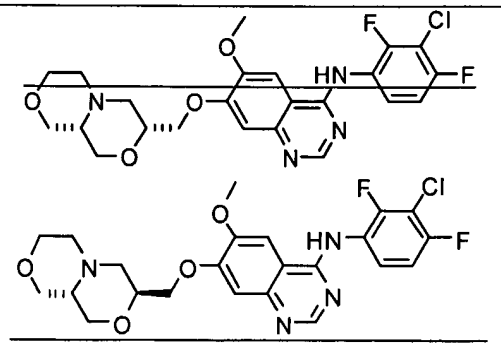
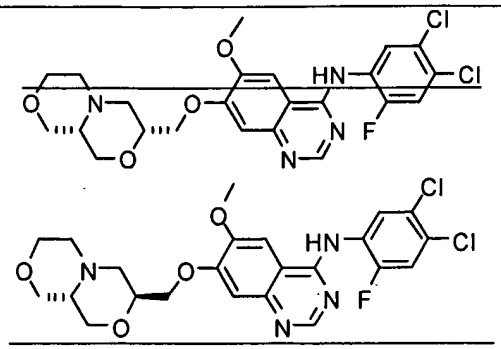
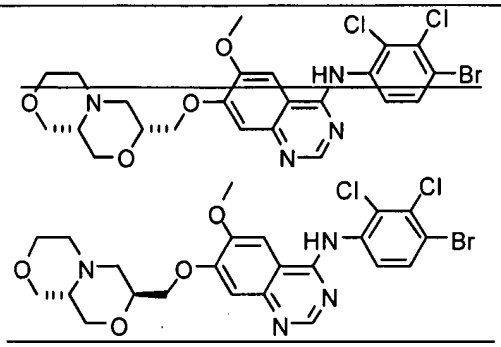
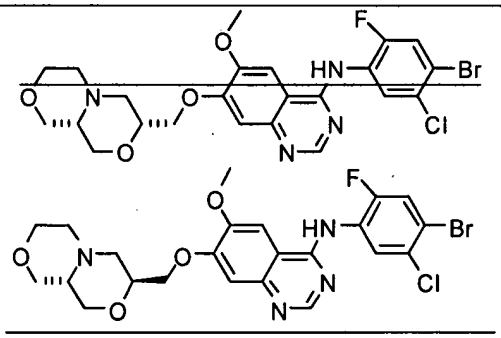
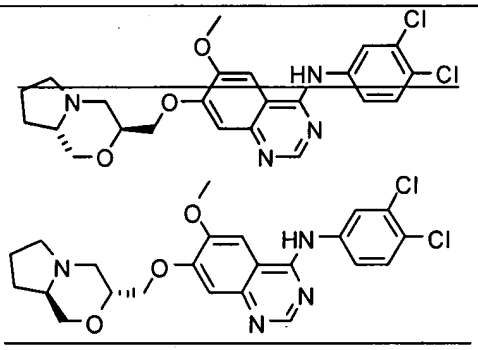
17	N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3aR,5r,6aS)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine; N-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-({[(3aR,6aS)-2-(2-methylpropyl)octahydrocyclopenta[c]pyrrol-5-yl]methyl}oxy)quinazolin-4-amine	
22	N-(3,4-dichloro-2-fluorophenyl)-7-{[(3S,9aS)-hexahydro-1H-[1,4]oxazino[3,4-c][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine	
23	N-(4-bromo-3-chloro-2-fluorophenyl)-7-{[(3S,9aS)-hexahydro-1H-[1,4]oxazino[3,4-c][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine	
24	N-(3-chloro-2,4-difluorophenyl)-7-{[(3S,9aS)-hexahydro-1H-[1,4]oxazino[3,4-c][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine	

Table 1

26	N-(4,5-dichloro-2-fluorophenyl)-7-{[(3S,9aS)-hexahydro-1H-[1,4]oxazino[3,4-c][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine	
27	N-(4-bromo-2,3-dichlorophenyl)-7-{[(3S,9aS)-hexahydro-1H-[1,4]oxazino[3,4-c][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine	
28	N-(4-bromo-5-chloro-2-fluorophenyl)-7-{[(3S,9aS)-hexahydro-1H-[1,4]oxazino[3,4-c][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine	
31	N-(3,4-dichlorophenyl)-7-{[(3R,8aR)-hexahydro-1H-pyrrolo[2,1-c][1,4]oxazin-3-ylmethyl]oxy}-6-(methyloxy)quinazolin-4-amine	

Please replace paragraphs [0081]-[0089] found on page 69 of the Specification with the following amended paragraphs.

[0081] Embodiment 81: Another aspect of the invention is a pharmaceutical composition comprising a compound according to any one of ~~paragraphs~~embodiments [0024]-[0080] and a pharmaceutically acceptable carrier.

[0082] Embodiment 82: Another aspect of the invention is a metabolite of the compound ~~or the pharmaceutical composition~~, and optionally together with a pharmaceutically acceptable carrier, according to any one of ~~paragraphs~~embodiments [0024]-[0081].

[0083] Embodiment 83: Another aspect of the invention is a method of modulating the *in vivo* activity of a kinase, the method comprising administering to a subject an effective amount of the compound ~~or the pharmceutical composition~~, and optionally together with a pharmaceutically acceptable carrier, according to any of ~~paragraphs~~embodiments [0024]-[0081].

[0084] Embodiment 84: Another aspect of the invention is a method according to ~~paragraph~~embodiment [0083], wherein the kinase is selected from ephrin and EGFR.

[0085] Embodiment 85: Another aspect of the invention is a method of modulating the *in vivo* activity of a plurality of kinases, the method comprising administering to a subject an effective amount of the compound ~~or the pharmceutical composition~~, and optionally together with a pharmaceutically acceptable carrier, according to any of ~~paragraphs~~embodiments [0024]-[0081].

[0086] Embodiment 86: Another aspect of the invention is a method according to ~~paragraph~~embodiment [0085], wherein the plurality of kinases comprises at least one of ephrin and EGFR.

[0087] Embodiment 87: Another aspect of the invention is a method according to ~~paragraph~~embodiment [0084], wherein modulating the *in vivo* activity of the kinase comprises inhibition of said kinase.

[0088] Embodiment 88: Another aspect of the invention is a method according to ~~paragraph~~embodiment [0086], wherein modulating the *in vivo* activity of the plurality of kinases comprises inhibition of at least one of ephrin and EGFR.

[0089] Embodiment 89: Another aspect of the invention is a method of treating diseases or disorders associated with uncontrolled, abnormal, and/or unwanted cellular activities, the method comprising administering, to a mammal in need thereof, a therapeutically effective amount of the compound, and optionally together with a pharmaceutically acceptable carrier, as described in any one of ~~paragraphs~~embodiments [0024]-[0081].

On pages 75-76 of the Specification, please replace paragraph [0113] with the following amended paragraph.

[0113] "Optional" or "optionally" means that the subsequently described event or circumstance may or may not occur, and that the description includes instances where said event or circumstance occurs and instances in which it does not. It will be understood by those skilled in the art with respect to any group containing one or more substituents that such groups are not intended to introduce any substitution or substitution patterns (for example, substituted alkyl includes optionally substituted cycloalkyl groups, which in turn are defined as including optionally substituted alkyl groups~~, potentially *ad infinitum*~~) that are sterically impractical and/or synthetically non-feasible. "Optionally substituted" refers to all subsequent modifiers in a term, for example in the term "optionally substituted arylC_{1-8} alkyl," optional substitution may occur on both the "C_{1-8} alkyl" portion and the "aryl" portion of the molecule; and for example, optionally substituted alkyl includes optionally substituted cycloalkyl groups, which in turn are defined as including optionally substituted alkyl groups~~, potentially *ad infinitum*~~. Examples of optional substitution include, but are not limited to alkyl, halogen, alkoxy, hydroxy, oxo, carbamyl, acylamino, sulfonamido, carboxy, alkoxycarbonyl, acyl, alkylthio, alkylsulfonyl, nitro, cyano, amino, alkylamino, cycloalkyl and the like.

On page 97 of the Specification, please replace paragraph [0189] with the following amended paragraph.

[0189] 1,4:3,6-Dianhydro-2-*O*-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-5-*O*-(difluoromethyl)-L-iditol: ^{1}H NMR (400 MHz, d_6-DMSO): 9.64 (s, 1H), 8.56 (s, 1H), 8.26 (d, 1H), 7.86-7.82 (m, 2H), 7.77 (d, 1H), 7.31 (s, 1H), 6.84 (tr, 1H), 5.12 (br s, 1H), 4.74 (m, 2H), 4.06 (ddd AB, 2H), 3.98-3.90 (m, 6H); MS (EI) for $C_{22}H_{19}N_3O_5BrClF_2$: 558 ($MH^+$).

On pages 98 of the Specification, please delete paragraph [0194].

On page 101-103 of the Specification, please replace paragraphs [0202]-[0207] and the three lines preceding [0202] with the following.

Example 4
Methyl 3,6-anhydro-5-*O*-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy) quinazolin-7-yl]-2-*O*-methyl-α-~~D~~L-idofuranoside

[0202] To a mixture of 1,4:3,6-dianhydro-5-*O*-(phenylcarbonyl)-(D)-~~glycitol~~glucitol (4.32g, 17.3 mmol), triethylamine (4.91 mL, 35.3 mmol) and 4-dimethylaminopyridine (0.63g, 5.2 mmol) in dichloromethane (50 mL) at -10 ° to -15° was added trifluromethanesulfonic anhydride (3.48mL, 20.7 mmol) dropwise over ten minutes and the resulting mixture was stirred at this temperature for 3 hours. The mixture was poured into 100 mL of ice-water and extracted with dichloromethane (3 x 50 mL). The combined organic layers were washed with brine, dried over anhydrous sodium sulfate, filtered then concentrated. The crude triflate was suspended in toluene (50 mL) followed by addition of 1,8-diazabicyclo[4,5,0]undec-7-ene (5.25 mL, 34.6 mmol) and the mixture was stirred at room temperature for 18 hours. The reaction mixture was poured into ice-water and partitioned then the aqueous portion was extracted with dichloromethane (3 x 50 mL). The combined organic portion was washed with brine, dried over anhydrous sodium sulfate, filtered and concentrated. The residue was purified by flashed chromatography (silica gel, 5-20% ethyl acetate-hexane) to give 1,4:3,6-dianhydro-2-deoxy-5-*O*-(phenylcarbonyl)-~~L~~D-*arabino*-hex-1-enitol, as a white solid, 3.10g, 77% yield. ^{1}H NMR (400MHz; $CDCl_3$): 8.08-8.06 (m, 2H), 7.61-7.57 (m, 1H), 7.56-7.43 (m, 2H), 6.62-6.61 (d, 1H), 5.48-5.46 (m,1H), 5.32-5.26 (m,1H), 5.13-5.10 (m, 2H), 4.18-4.14 (tr,1H), 3.61-3.56 (tr, 1H).

[0203] Methyl 3,6-anhydro-5-*O*-(phenylcarbonyl)-β-~~L~~D-glucofuranoside: To a solution of 1,4:3,6-dianhydro-2-deoxy-5-*O*-(phenylcarbonyl)-~~L~~D-arabino-hex-1-enitol (1.00g, 4.3 mmol) in methanol (17 mL) at -4°C was added 3-chloroperoxybenzoic acid (85%, 1.35g, 8.6 mmol), and the resulting mixture was slowly warmed to room temperature and stirred

for 18 hours. The reaction mixture was concentrated, diluted with dichloromthane (50 mL), washed with saturated aqueous sodium bicarbonate solution, dried over sodium sulfate, filtered and concentrated. The residue was purified by flash chromatography (silica gel, 25-60% ethyl acetate-hexane) to give methyl 3,6-anhydro-5-*O*-(phenylcarbonyl)-β-~~L~~D-glucofuranoside as a white solid, 1.03g, 83% yield. ^{1}H NMR (400MHz; $CDCl_3$): 8.11-8.08 (d, 2H), 7.61-7.56 (tr, 1H), 7.48-7.44 (m, 2H), 5.24-5.17 (m, 2H), 4.96 (s, 1H), 4.57-4.56 (d, 1H), 4.27 (s, 1H), 4.22-4.18 (dd, 1H), 4.08-4.04 (dd, 1H) 3.36 (s, 3H).

[0204] Methyl 3,6-anhydro-2-*O*-methyl-5-*O*-(phenylcarbonyl)-β-~~L~~D-glucofuranoside: A mixture of methyl 3,6-anhydro-5-*O*-(phenylcarbonyl)-β-~~L~~D-glucofuranoside (1.03g, 3.7 mmol), silver (I) oxide (0.85g, 3.7 mmol) and methyl iodide (0.34 mL, 5.5 mmol) in DMF (2 mL) was heated at 60°C for 1 hour. After cooling to room temperature the reaction mixture was diluted with ethyl acetate (50 mL), filtered over celite, adsorbed on silica gel (10g) and purified by flash chromatography (silica gel, 5-30% ethyl acetate-hexane) to give methyl 3,6-anhydro-2-*O*-methyl-5-*O*-(phenylcarbonyl)-β-~~L~~D-glucofuranoside as a colorless oil, 0.82g, 76% yield. ^{1}H NMR (400MHz; $CDCl_3$): 8.11-8.09 (d, 2H), 7.60-7.56 (m, 1H), 7.46-7.44 (m, 2H), 5.24-5.20 (m, 1H), 5.18-5.09 (tr, 1H), 4.99 (s, 1H), 4.61-4.60 (d, 1H), 4.21-4.17 (tr, 1H), 4.08-4.03 (tr, 1H), 3.81 (s, 1H), 3.40 (s, 3H), 3.57 (s, 3H).

[0205] Methyl 3,6-anhydro-2-*O*-methyl-~~α-~~β-D-~~ido~~glucofuranoside: A solution of methyl 3,6-anhydro-2-*O*-methyl-5-*O*-(phenylcarbonyl)-β-~~L~~D-glucofuranoside (820mg, 3.1mmol) and 50% sodium hydroxide (248 mg, 3.1 mmol) in methanol (10mL) was stirred at room temperature for 30 minutes. The material was adsorbed on silica gel (5g) and passed through a short column (15% ethyl acetate in hexanes to 5% methanol in ethyl acetate) to give methyl 3,6-anhydro-2-*O*-methyl-~~α-~~β-D-~~ido~~glucofuranoside as a colorless oil, 420 mg, 85% yield. ^{1}H NMR (400MHz; $CDCl_3$): 5.04 (s, 1H), 5.84-5.81 (tr, 1H), 4.44-4.42 (tr, 1H), 4.25-4.19 (m, 1H), 3.85-3.75 (m, 1H), 3.49 (s, 3H), 3.43 (s, 3H), 2.75-2.72 (d, 1H).

[0206] Methyl 3,6-anhydro-2-*O*-methyl-5-*O*-(methylsulfonyl)-β-L-glucofuranoside: Methyl 3,6-anhydro-2-*O*-methyl-~~α-~~β-D-~~ido~~glucofuranoside (420 mg, 2.6 mmol) was

dissolved in dichloromethane (10 mL) and pyridine (0.36 mL, 3.7 mmol) at 0°C. Methanesulfonyl chloride (0.14 mL, 3.1 mmol) was added and the resulting mixture was stirred at 0°C for 1 hour then at room temperature for 2 hours. The reaction mixture was washed with water and saturated aqueous sodium bicarbonate solution, dried over anhydrous sodium sulfate, filtered and concentrated to give methyl 3,6-anhydro-2-*O*-methyl-5-*O*-(methylsulfonyl)-β-~~L~~D-glucofuranoside as a colorless oil, 669mg, 95% yield, which was used without further purification.

[0207] Methyl 3,6-anhydro-5-*O*-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy) quinazolin-7-yl]-2-*O*-methyl-α-~~D~~L-idofuranoside: Methyl 3,6-anhydro-2-*O*-methyl-5-*O*-(methylsulfonyl)-β-~~L~~D-glucofuranoside (314 mg, 1.1 mmol) was dissolved in DMF (3mL). To this solution was added potassium carbonate (404 mg, 2.9 mmol) and 4-[(4-bromo-3-chlorophenyl)amino]-6-methyloxy-7-hydroxyquinazoline trifluoroacetate (280 mg, 0.59 mmol). The resulting mixture was heated at 135°C for 18h. After cooling to room temperature the reaction mixture was diluted with ethyl acetate (15 mL), washed with water, dried over anhydrous sodium sulfate, filtered and concentrated. The residue was purified by flash chromatography (silica gel, 2-7% methanol in 1:1 ethyl acetate:hexanes) to give methyl 3,6-anhydro-5-*O*-[4-[(4-bromo-3-chlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-2-*O*-methyl-α-~~D~~L-idofuranoside as a white solid, 181 mg, 28% yield. ^{1}H NMR (400MHz; Methanol-d_4): 8.75 (s, 1H), 8.04–8.06 (d, 1H), 7.99 (s, 1H), 7.78-7.75 (d, 1H), 7.64-7.61 (d, 1H), 7.35 (s, 1H), 5.16-5.14 (d, 1H), 5.02 (s, 1H), 4.89 (br, 1H), 4.69-4.68 (d, 1H) 4.46-4.42 (dd, 1H), 4.09 (br, 1H), 4.06 (s, 3H), 3.69(s, 1H), 3.48(s, 3H), 3.42 (s, 3H); MS (EI) for $C_{23}H_{23}BrClN_3O_6$: 551.88 (MH^+).

On page 103-105 of the Specification, please delete Example 5 which encompasses paragraphs [0208]- [0211] and the three lines which precede paragraph [0208].

On page 117 of the Specification, please replace paragraph [0248] with the following amended paragraph.

[0248] (3*S*,-8a*S*)-3-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}-methyl)hexahydropyrrolo[1,2-a]pyrazin-1(2H)-one: ^{1}H NMR (400 MHz, d_4-MeOH): 8.36 (s, 1H), 7.71 (s, 1H). 7.60-7.55 (m, 2H), 7.18 (s, 1H), 4.29-4.22 (m, 1H), 4.19-4.14 (m, 1H), 4.02 (s, 3H), 3.99-3.92 (m, 1H), 3.36-3.30 (m, 1H), 3.32-3.90 (m, 2H), 2.82-2.74 (m, 1H), 2.26-2.10 (m, 1H), 2.19-2.18 (m, 3H), 1.30-1.20 (m, 2H), 0.90-0.80 (m, 1H); MS (EI) for $C_{23}H_{23}BrClN_5O_3$: 551 (MH^+).

On page 120 of the Specification, please replace paragraph [0260] with the following.

[0260] *N*-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3a*R*,5*r*,6a*S*)-octahydrocyclo-penta[*c*]pyrrol-5-yl]methyl]oxy}quinazolin-4-amine hydrochloride: 1,1-Dimethylethyl (3a*R*,6a*S*)-5-({[4-[(3,4-dichloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]-oxy}methyl)hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate was taken up in methanol (10 mL) and treated with 4.0M hydrogen chloride in dioxane (excess) and heated briefly to reflux. Concentration *in vacuo* provided ~~*N*-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3a*R*,5*r*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-5-yl]methyl]oxy}quinazolin-4-amine hydro-chloride.~~ *N*-(3,4-dichloro-2-fluorophenyl)-6-(methyloxy)-7-{[[(3a*R*,5*r*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-5-yl]methyl]oxy}quinazolin-4-amine hydro-chloride. MS (EI) for ~~$C_{28}H_{31}Cl_2FN_4O_4$~~: $C_{23}H_{23}Cl_2FN_4O_2$: 477, 479 (MH^+).

On pages 124-125 of the Specification, please replace paragraph [0274] and the three lines preceding it with the following.

Example 17

Ethyl (3a*R*,5*r*,6a*S*)-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy) quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate hydrochloride

[0274] Ethyl (3a*R*,5*r*,6a*S*)-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy) quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate hydrochloride: A solution of *N*-(4-bromo-3-chloro-2-fluorophenyl)-6-(methyloxy)-7-{[(3a*R*,5*r*,6a*S*)-octahydrocyclopenta[*c*]pyrrol-5-ylmethyl]oxy}quinazolin-4-amine hydrobromide (0.050 g, 0.0830 mmol), triethylamine (0.046 mL, 0.0332 mmol) in 2.0 mL dichloromethane was cooled to 0°C and ethyl chloridocarbonate (0.010 mL, 0.0913 mmol) was added. The solution was stirred for 0.5 h at low temperature and quenched with saturated aqueous sodium bicarbonate. The reaction mixture was then partitioned between dichloromethane and saturated aqueous sodium bicarbonate. The layers were separated and the aqueous layer was extracted with dichloromethane (2 x 75 mL). The combined organic layers were dried over anhydrous sodium sulfate, filtered and concentrated *in vacuo*. Column chromatography (SiO_2, 5% methanol in dichloromethane), followed by treatment in methanol with 4.0 M hydrogen chloride in dioxane (0.05 mL) and concentration provided ethyl (3a*R*,5*r*,6a*S*)-5-({[4-[(4-bromo-3-chloro-2-fluorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy}methyl)hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate hydrochloride (27.7 mg, 53% yield). ^{1}H NMR (400 MHz, d_4-MeOH): 8.59 (s, 1H), 7.83 (s, 1H), 7.60 (d, 1H), 7.41 (t, 1H), 7.12 (s, 1H), 4.14 (d, 2H), 4.11 (m, 2H), 4.09 (s, 3H), 3.45 (dd, 2H), 3.30 (dd, 2H), 2.67 (m, 2H), 2.58 (m, 1H), 2.12 (m, 2H), 1.74 (m, 1H), 1.36 (m, 2H), 1.18 (t, 3H); MS (EI) for $C_{26}H_{27}N_4O_4FClBr$: 595 (MH^+).

On page 125-127 of the Specification, please replace paragraphs [0278]-[0282] and the three lines preceding paragraph [0278] with the following.

Example 18

***N*-(3,4-dichlorophenyl)-7-({[(3a*R*,~~5*r*~~,6a*S*)-2-methyloctahydrocyclopenta[*c*]pyrrol-5-yl]}oxy)-6-(methyloxy)quinazolin-4-amine hydrochloride:**

[0278] 1,1-Dimethylethyl (3a*R*,6a*S*)-5-(hydroxy)-hexahydrocyclopenta[*c*] pyrrole-2(1*H*)-carboxylate: Sodium borohydride (0.15 g, 4.00 mmol), was added to a solution of 1,1-dimethylethyl (3a*R*,6a*S*)-5-oxo-hexahydrocyclopenta[*c*] pyrrole-2(1*H*)-carboxylate (0.45 g, 2.00 mmol) in 10 mL methanol at 0°C and the reaction mixture was stirred for 1 h at this temperature. The solvent was evaporated, the crude mixture was diluted with 100 mL ethyl acetate and washed with water (30 mL), 1M aqueous hydrochloric acid and brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated to give 1,1-dimethylethyl (3a*R*,6a*S*)-5-(hydroxy)-hexahydrocyclopenta[*c*] pyrrole-2(1*H*)-carboxylate (0.44g, 98%). ^{1}H NMR (400 MHz, d_6-DMSO): 4.08 (m, 1H), 3.40 (m, 2H), 3.30 (m, 2H), 2.50 (m, 2H), 1.98 (m, 2H), 1.40 (s, 9H), 1.30 (m, 2H). MS (EI) for $C_{12}H_{21}NO_3$: 228 (MH^+).

[0279] 1,1-Dimethylethyl (3a*R*,6a*S*)-5-{[(methylsulfonyl)oxy]}hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate: Methanesulfonyl chloride (0.18 mL, 2.33 mmol), was added dropwise to a solution of 1,1-dimethylethyl (3a*R*,6a*S*)-5-(hydroxy)-hexahydrocyclopenta[*c*] pyrrole-2(1*H*)-carboxylate (0.44 g, 1.94 mmol) and triethylamine (0.81 mL, 5.81 mmol) in 10 mL dichloromethane at 0°C and the reaction mixture was stirred for 1 h at room temperature. The solvent was evaporated, the resulting crude mixture was diluted with 100 mL ethyl acetate and washed with water (30 mL), brine, 1M aqueous hydrochloric acid and brine again. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated. The resulting crude 1,1-dimethylethyl (3a*R*,6a*S*)-5-{[(methylsulfonyl)oxy]}hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate was used without further purification. MS (EI) for $C_{13}H_{23}NO_5S$: 306 (MH^+).

[0280] 1,1-dimethylethyl (3a*R*,6a*S*)-5-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy) quinazolin-7-yl]oxy})hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate: A solution of 4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-ol trifluoroacetate (salt) (0.22 g, 0.49mmol), 1,1-dimethylethyl (3a*R*,6a*S*)-5-{[(methylsulfonyl)oxy]}hexahydro-cyclopenta[*c*]pyrrole-2(1*H*)-carboxylate (0.15 g, 0.45 mmol), potassium carbonate (0.34 g, 2.50 mmol) in N,N-dimethylacetamide (5 mL) was heated in a sealed reaction tube at 90°C for 12 h. The crude reaction mixture was diluted with 100 mL 10% methanol in ethyl acetate and washed with saturated aqueous sodium bicarbonate (1x 30 mL), water (1 x 30 mL) and brine (1 x 30 mL). The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated. Column chromatography (SiO_2, 3:2 hexanes:acetone) provided 1,1-dimethylethyl (3a*R*,6a*S*)-5-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy})hexahydrocyclopenta[*c*]pyrrole-2(1*H*)-carboxylate (0.23 g, 98%). ^{1}H NMR (400 MHz, d_6-DMSO): 9.57 (s, 1H), 8.52 (s, 1H), 8.24 (d, 1H), 7.88 (dd, 1H), 7.78 (s, 1H), 7.62 (d, 1H), 7.13 (s, 1H), 5.15 (m, 1H), 3.96 (s, 3H), 3.42 (m, 2H), 3.36 (m, 2H), 2.80 (bs, 2H), 2.06 (m, 2H), 1.94 (m, 2H), 1.40 (s, 9H). MS (EI) for $C_{27}H_{30}Cl_2N_4O_4$: 547 (MH^+).

[0281] *N*-(3,4-dichloro-phenyl)-6-(methyloxy)-7-{[(3a*R*,~~5*r*~~,6a*S*)-octahydrocyclo-penta[*c*]pyrrol-5-yl]oxy} quinazolin-4-amine hydrochloride: 1,1-Dimethylethyl (3a*R*,6a*S*)-5-({[4-[(3,4-dichlorophenyl)amino]-6-(methyloxy)quinazolin-7-yl]oxy})hexahydrocyclo-penta[*c*]pyrrole-2(1*H*)-carboxylate (0.23 g, 0.42 mmol) was taken up in methanol (10 mL) and treated with 4.0M hydrogen chloride in dioxane (excess) and heated briefly to reflux. Concentration *in vacuo* provided *N*-(3,4-dichloro-phenyl)-6-(methyloxy)-7-{[(3a*R*,~~5*r*~~,6a*S*)-octahydrocyclopenta[*c*]pyrrol-5-yl]oxy} quinazolin-4-amine hydrochloride (0.20 g, 100%). MS (EI) for $C_{22}H_{22}Cl_2N_4O_2$: 445 (MH^+).

[0282] *N*-(3,4-Dichlorophenyl)-7-({[(3a*R*,~~5*r*~~,6a*S*)-2-methyloctahydrocyclopenta[*c*]pyrrol-5-yl]}oxy)-6-(methyloxy)quinazolin-4-amine hydrochloride: *N*-(3,4-Dichloro-phenyl)-6-(methyloxy)-7-{[(3a*R*,~~5*r*~~,6a*S*)-octahydrocyclopenta-[*c*]pyrrol-5-yl]oxy}quinazolin-4-amine hydrochloride (0.20 g, 0.42 mmol) was solubilized in formic acid (5.0 mL) and 37% aqueous formaldehyde (1 mL)

was added. The solution was heated to 95°C for 12 h. The reaction mixture was concentrated *in vacuo*. The residue was taken up in a mixture of 10% methanol in ethyl acetate (100 mL) and washed with saturated aqueous sodium bicarbonate (2x 30 mL) and brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated. The residue was purified by HPLC (reverse-phase, acetonitrile/water/0.1% TFA). Upon removal of solvent the product was taken up in a mixture of 10% methanol in ethyl acetate (100 mL) and washed with saturated aqueous sodium bicarbonate (2x 30 mL) and brine. The organic layer was dried over anhydrous sodium sulfate, filtered and concentrated then the product was taken up in methanol and treated with 4.0 M hydrogen chloride in dioxane (1eq.). Removal of solvent *in vacuo* provided 116 mg (56%) of *N*-(3,4-dichlorophenyl)-7-({[(3a*R*,~~5*r*~~,6a*S*)-2-methyloctahydrocyclopenta[*c*]pyrrol-5-yl]}oxy)-6-(methyloxy)quinazolin-4-amine hydrochloride. ^{1}H NMR (400 MHz, d_6-DMSO): 11.05 (bs, 1H), 8.90 (s, 1H), 8.44 (s, 1H), 8.18 (d, 1H), 7.84 (dd, 1H), 7.76 (s, 1H), 7.48 (s, 1H), 5.30 (m, 1H), 4.00 (s, 3H), 3.35 (m, 2H), 2.90 (m, 2H), 2.24 (m, 5H), 2.10 (m, 2H), 1.24 (m, 2H). MS (EI) for $C_{23}H_{24}Cl_2N_4O_2$: 459, 461 (MH^+).

On pages 139-147 of the Specification, please delete paragraphs [0317]-[0371].

On page 157-158 of the Specification, please replace paragraph [0411] with the following amended paragraph.

[0411] N-(3,4-dichlorophenyl)-7-[({3-[(dimethylamino)methyl]-1,2,4-oxadiazol-5-yl}methyl)oxy]-6-(methyloxy)quinazolin-4-amine: ^{1}H-NMR (400MHz; DMSO-d_6): 10.48 (br s,1H), 8.75 (s, 1H), 8.20 (s, 1H), 8.05 (s, 1H), 7.81 (d, 1H), 7.72 (d, 1H), 7.25 (s, 1H), 5.85 (s, 2H), 4.85 (s, 2H), 4.00 (s, 3H), 2.88 (s, 6H); MS (EI) for $C_{21}H_{20}N_6O_3Cl_2$: 475 (MH^+).

Please delete the following entries in Table 3, entries 2, 3, 4, 5, 6, 7, 31, 33, 34, 35, 37, 45, 47, 48, and 50 found on pages 170-171, 173, and 174 of the Specification. Please delete Table 4, encompassing entries 1-54 found on pages 176-180 of the Specification. Please delete entry 252 in Table 6 found on page 200 of the Specification.